UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,179	09/10/2001	Satoru Okamoto	213701US0PCT	9582

22850 7590 11/24/2004

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,179	OKAMOTO ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-14* is/are pending in the application.

4a) Of the above claim(s) *8-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/3/04 has been entered.

Status of Claims

Claims 1 and 3-14 are pending in the application.

Claim 2 has been cancelled in the Amendment of 9/22/03.

Claims 8-14 are withdrawn from consideration as being drawn to nonelected invention.

Claims 1 and 3-7 are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3-7, as amended, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method utilizing a phage random peptide library of structure as recited in e.g., page 29 and a substance that inhibits a nonstructural protein 3, HCV serine protease (NS3 protease) as the biomolecule and E.coli as the organism does not reasonably provide enablement for a method of screening any type of substance that interacts with any biomolecule using any type of peptide library or organism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons advanced in the last Office action (5/21/03 and 12/12/03).

Response to Arguments

Applicants submit that the general steps correlating to steps (a) through (e) in Claim 1 may be performed based on ordinary methods known to the skilled artisan. Applicants argue that several references were submitted that showed that the general methods for selection of a recombinant organisms that interacts with a biomolecule (generally steps (a) - (c) of Claim 1) would be well within the purview of the skilled artisan. It is further argued that the examiner points to these references and notes that depending on the components used in these references the conditions are different. In making this assertion it appears that the Examiner is overlooking MPEP 2164.06 and the fact that some experimentation is permissible (e.g., optimization based on the specific components employed).

In response, the references submitted by applicants and relied upon ***e.g.***, the Boublik et al reference, in fact teaches several limitations in using even a single organism for already a very specific protein. Boublik states that the ability to directly select genetic changes resulting in a desired phenotype is a powerful technique limited only by the ability of such systems to present functional proteins and the number of mutants capable of simultaneous presentation. Prokaryotic expression

places a restriction on the type of protein to which this technology can be applied. Eukaryotic proteins often require complex folding and glycosylation for functional activity. Théy are seldom expressed successfully in bacteria, in part due to the absence of the appropriate post-translational pathways when compared to their normal cellular environment, referring to reference 5. These limitations are apparent from the other cited references. These references describe specific method steps utilizing specific components therein. None of the references as so much mention that the specific methods used therein has found applicability to a general method using general components, as the instant claimed method. Additionally, it is well known in the art that the method of phage technology is limited to only naturally occurring amino acids and little is known about the effect of the phage environment, as well as contaminants from cellular debris and phage. There are also the difficulties in enriching positive clones where avidity effects arise due to multivalent binding of the phage and the general tendency of phage to contain two or more copies of the displayed polypeptide. The binding to the target immobilized on a solid phase depends not only on molecular affinity but also on other factors such as surface characteristics, number of attachment points(avidity effects), and hydrodynamic conditions and other

unpredictable factors or effects. To determine even a single component in a general method such that the object of the claim can be accomplished and avoid the pitfalls encountered in each of the cited prior art requires more than "some experimentation". Rather, it requires an undue amount of experimentation. The claims recite far too numerous undefined components/factors of the method. Thus, applicants' disclosure describing a defined (single) components used in the method would not suffice as enabling disclosure for the scope of the broad claimed method. The method does not recite a component of defined structure. It is not seen how the method can be manipulated without reciting the kind e.g., library of the different libraries used in the method. Applicants' disclosure simply invites one to experiment in the hope that a discovery can be made.

Claims 1 and 3-7, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons as set forth in the last Office action (12/12/03).

Response to Arguments

Applicants note that the specification at page 49 clearly states that the candidate inhibitory substance is a "compound in a chemical library." Applicants further argue that the specifics of how to make the chemical compound library or the compounds therein are not limiting. It is argued that the point of the present invention is to screen large chemical compound libraries (e.g., a combinatorial library) by the inventive method to identify specific substances that interacts with a specific region of a biomolecule to regulate the activity of the same. It is also argued that the present invention provides a general method of identifying lead compounds from a chemical compound library based on the compounds ability to disrupt a preformed interaction between a peptide displayed on the surface of a recombinant organism and a biomolecule binding to the same. The methods of making the chemical compound library or the compounds encompassed in the library are not limiting.

In response, it is not readily apparent from the disclosure the compounds covered by a chemical compound library, even assuming its method of making may not be limiting. As applicants stated above the specification provides a **general** method of identifying lead compounds. But fails to provide a description of the general method that leads to any compound in a chemical

library e.g., of any structural formulae. The compound in a chemical library is but one of the numerous and infinite components of the claimed compound without any definite structure/formula. There is not a single defined component of the claimed method in terms of any peptide library contacted with any recombinant organisms and a compound chemical library. The specification appears to cover all recombinant organisms, all peptide library and all types of inhibitory chemical compound. Claims drawn to the use of known chemical compounds must have a corresponding written description only so specific as to lead one to that class of compounds. In re Herschler (CCPA 1979) 200USPQ 711. A "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993. See further the decision in University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003). Thus, at the time of applicants' invention, it appears that applicants are not in possession of the genus components as used in the general steps of the method.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 3, 4, 5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Bottger et al (Oncogene).

Bottger discloses at pages 2141, Results section, a method

comprising preparing a phage peptide library of 6, 12 and 15-mer, contacting the phage peptide library (Table 1, page 2142) with mdm2 (biomolecule as claimed), selecting from the peptide library the peptides that bound to the biomolecule and assaying by ELISA the inhibitory effect of free peptides obtained from the phage clones and p53 with Pro or Tyr mutation (page 2143, col. 2) that inhibit the binding of mdm2 to p53. See further the specific method steps at page 2145, Materials and methods section.

Claims 1 and 3-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Fowlkes et al (USP 6,617,114).

Fowlkes discloses cols. 153-154, a method of identifying a ligand (a peptide library as instantly claimed) which can mediate the biological activity of a target protein (biomolecule, as claimed) via inhibition of the binding of a target protein to a binding partner ligand which comprises (a) screening a first combinatorial library comprising a plurality of first member ligands (peptide library, as claimed) for binding to the target protein, thereby identifying one or more target-binding ligands, (b) screening a second library comprising a plurality of second member ligands (substance as claimed) for the ability to inhibit the binding of one or more of said target-binding ligands to said target protein, thereby

obtaining one or more inhibitory ligands, and (c) determining which of the inhibitory ligands can mediate a biological activity of the target protein, said inhibitory ligand thereby being identified as an activity-mediating ligand, in which the target protein is a nuclear receptor of the steroid receptor family, in which the first library is composed of peptides, the peptides do not comprise antibody-like domains, at least one peptide is characterized by an amino acid sequence comprising the Leu-Xaa-Xaa-Leu-Leu sequence motif, wherein Xaa represents any genetically encoded amino acid, and the peptides are displayed on phage, and in which the second library is a non-biopolymeric combinatorial library e.g., benzodiazepine library. The target protein is an estrogen receptor. See further col. 5, line 50 up to col. 7, line 42 and the Examples at e.g., col. 35, Example 1 up to col. 47, line 37. Accordingly, the broad claimed method is fully met by the specific method of Fowlkes which recites specific components used in the method.

In view of the newfound art, above, applicants' arguments over the prior art e.g., Martens or O'Neil are moot.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Rosenberg et al discloses peptide ligands of the urokinase receptor.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner

Art Unit 1639

Tdw
November 22, 2004